REMARKS

In response to the PTO 948 provided with the Office Action dated March 28, 2001, Applicants respectfully submit that correction of drawings will be furnished upon allowance of the present invention.

IN THE CLAIMS:

Claims 46-72 are currently pending. Support for such new claims can be found throughout the specification. Claims 21-45 have been cancelled without prejudice to future prosecution and Applicants reserve full rights to pursue this subject matter in related applications.

I. Elected subject matter

In the Office Action, the Examiner states that claims 22-45 corresponds to non-elected subject matter, and is thus withdrawn from consideration. Specifically, the Examiner alleges that the claims reciting polypeptide sequences or deposit clone reference numbers do not correspond to originally-elected subject matter, which is allegedly limited to a list of SEQ ID NOs corresponding to the claimed nucleic acid sequences. Applicants respectfully assert that these claims indeed correspond to the originally-elected subject matter, as discussed below. Further, Applicants respectfully submit that the clone names and corresponding ATCC deposit numbers recited in the claims have been specifically disclosed in Table VII and Table VI, respectively, and clearly correspond to the elected subject matter.

With respect to nucleic acids encoding the recited protein sequences, Applicants note that claims drawn to this subject matter were grouped with the elected nucleic acid claims in the Restriction Requirement of January 31, 2000, were among those claims presented in a Preliminary Amendment submitted with the Response to Restriction Requirement on April 3, 2000, and were examined in the Office Action dated June 28, 2000. Specifically, original claim 7 is directed to nucleic acids encoding any of a number of SEQ ID NOs, including 167, 177, 179, and 225. Claim 7 was included in Group I in the Restriction Requirement of January 31, 2000, which was elected in the Response of April 3, 2000. Further, this claim was examined, in the Office Action of June 28, 2000. Therefore, such claims have been part of the elected invention and have already been examined.

In view of the above, Applicants respectfully submit that each of the claims 21-45 and newly added claims 46-72 indeed correspond to elected subject matter, and urge the Examiner to review these claims accordingly.

II. Rejections under 35 U.S.C. § 101

Claim 21 was rejected under 35 U.S.C. § 101 for allegedly lacking utility. Specifically, the Examiner states that, first, no indication exists as to what is the mature form of each protein, and, second, no patentable utility is allegedly provided for the nucleic acids corresponding to SEQ ID NOs:76, 78, or 124. Applicants respectfully traverse this rejection.

In making this rejection, the Examiner first states that while the claimed polynucleotides are asserted as encoding the full length polypeptides, "No indication exists in this or any other part of the specification which would guide the person wishing to practice the invention such that he would know what the mature forms of the proteins are or which portion(s) constitute signal peptides nor what the function of the peptides are that the DNA encoded" (page 5, lines 14-17 of present Office Action). The Examiner also raises the possibility that multiple rounds of signal sequence processing of the present proteins may occur. The Examiner's assertion that no mature or signal peptides have been provided is incorrect. Both Tables IV and V of the specification, as well as the sequence listing, provide exactly that information. Moreover, Applicants clearly addressed this issue in the Amendment filed December 22, 2000 (See, e.g., page 9 of the Amendment). Further, regarding the alleged possibility that multiple rounds of signal sequence processing may occur, the Examiner has provided no evidence whatsoever that this may be the case with the present proteins. Simply providing two examples of proteins where this happens does not mean that this is likely to be the case with the present proteins. Unless the Examiner can provide a prima facie case to the contrary, Applicants respectfully submit that the Examiner must accept the asserted signal peptides and mature peptides presently disclosed.

Regarding the function of the claimed polynucleotides, the Examiner alleges that no patentable utility is provided for the polynucleotides of SEQ ID NO:76, 78, and 124. In particular, the Examiner attaches much significance to the language used in the specification, for example, that the protein encoded by SEQ ID NO:76 "may" be useful. The Examiner allegedly prefers the specification to say that the protein "is useful" for the disclosed purpose, however, no legal justification for this emphasis on the particular language used in the application to describe the utility of the protein is provided. Applicants respectfully submit that Merriam-Webster's

Online Collegiate® Dictionary (http://www.m-w.com) defines "may" as "have the ability to" and that "may" is sometimes used interchangeably with "can". Furthermore, Applicants assert that, regardless of the specific language used. Further, the specification provides a clear assertion as to the possible uses of the claimed sequences. According to the "Guidelines for Examination of Applications for Compliance with the Utility Requirement" on the USPTO website:

> "If the applicant has asserted that the claimed invention is useful for any particular purpose (i.e., a "specific utility") and that assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility. Credibility is to be assessed from the perspective of one of ordinary skill in the art in view of any evidence of record (e.g., data, statements, opinions, references, etc.) that is relevant to the applicant's assertions. An applicant must provide only one credible assertion of specific utility for any claimed invention to satisfy the utility requirement." (http://www.uspto.gov/web/offices/pac/dapp/oppd/utility.htm#guide)

Furthermore,

> "To properly reject a claimed invention under 35 U.S.C. § 101, the Office must (a) make a prima facie showing that the claimed invention lacks utility, and (b) provide a sufficient evidentiary basis for factual assumptions relied upon in establishing the prima facie showing. If the Office cannot develop a proper prima facie case and provide evidentiary support for a rejection under § 101, a rejection on this ground should not be imposed.
> (http://www.uspto.gov/web/offices/pac/dapp/oppd/utility.htm#initial)

According to the MPEP as well as the recently-published Training Materials, even when ***no*** utility is asserted, a sequence may still have a "well established utility", which is defined as a specific, substantial, and credible utility which is "well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art." Indeed, Applicants submit that the specification as filed clearly provides a utility for each of these sequences (e.g. in the treatment or diagnosis of cancer or neurodegenerative disorders such as Alzheimer's Disease for SEQ ID NO:76), and assert that the utility of the claims should be assessed on this basis.

Further, regarding SEQ ID NO:76, the specification clearly suggests that this protein is a Kunitz protease inhibitor. Applicants respectfully submit that Kunitz protease inhibitors had a well-established utility at the time of the filing of the present application. For example, various studies had shown that administration of the Kunitz protease inhibitor Tissue factor pathway inhibitor (TFPI) can inhibit the toxicity associated with *E. coli* infection. TFPI has been successfully used to prevent lethality and attenuate coagulapathic responses in a baboon model of septic shock (see, enclosed Exhibit I: Creasey *et al.*, J. Clin. Invest. (1993) 81:2850, and Exhibit

II: Carr *et al.* Circ. Shock (1995) 44:126). In response to the Examiner's statement that the assertion regarding Kunitz protease inhibition is not persuasive on the basis of no factual scientific data demonstrating inhibition, Applicants remind the Examiner that they are under no requirement to provide any evidence to support an asserted function. Instead, if the Examiner wishes to question this asserted function, it is the Examiner's burden to establish a prima facie case as to why the function may not be true. See, e.g., MPEP § 2107.01-IV.

Concerning SEQ ID NO:78, the specification clearly states that the protein is a novel colipase homolog which can be used in the treatment or diagnosis of a number of diseases including hyperlipidemia, hypercholesterolemia, atherosclerosis, cardiovascular disorders, neurodegenerative disorders, and disorders linked to male fertility. Again, the Examiner improperly bases this rejection on the fact that the specification uses the phrase "may be" when describing the function of the gene, and because no experimental data is presented. As discussed supra, the precise wording used to assert a function is not relevant to utility under §101, and it is the Examiner's burden to establish a prima facie case questioning the credibility of any such function with scientific evidence or reasoning. In the absence of such a prima facie case, Applicants are under no obligation to provide evidence regarding the asserted function.

Further, at the time of filing of the application, colipases had a well established utility. Specifically, colipases were known to be important components of pancreatic enzyme supplements, are were also useful in the diagnosis of acute pancreatitis. (see, e.g., enclosed Exhibit III: Lott *et al.* Clin. Chem. (1986) 32:1290-1302). Therefore, at the time of filing, even if the specification had not provided a number of specific utilities for the sequence relating to the diagnosis and treatment of various diseases, the utility requirement was satisfied by the identification of the sequence as encoding a homolog of colipase, which had a well established utility at the time of filing.

Finally, concerning SEQ ID NO: 124, this sequence is clearly identified as a novel phosphatidylethanolamine binding protein, and to be useful in the diagnosis or treatment of cancer, neurodegenerative diseases, and disorders related to male fertility and sterility.

In addition, at the time of filing, phosphatidylethanolamine binding proteins (PBPs) had well-established utilities. For example, the first PBP to be identified, PBP1, was also called hippocampal cholinergic neurostimulating peptide (HCNP), which was known to enhance the secretion of acetylcholine by neurons in the hippocampus (Tohdoh *et al.*, Brain Res. Mol. Brain Res. (1995) 30:381-384). In addition, HCNP was shown to be associated with the presence of

Hirano bodies thought to be related to memory impairment in Alzheimer's disease (see enclosed Exhibit IV: Mitake *et al.*, Neuropathol. Appl. Neurobiol. (1995) 21:35-40, and Exhibit V: Abstract of Mitake *et al.*, Kaohsiung J. Med. Sci (1997) 13:10-18). In view of the number of diseases involving acetylcholine dysfunction in neurons (e.g. Schizophrenia, epilepsy, neuropathies), the role of the present protein in enhancing acetylcholine secretion would have had clear utility to one of skill in the art at the time of filing.

Thus, Kunitz protease inhibitors, colipases, and phosphatidylethanolamine binding proteins, to which the polypeptides encoded by the claimed nucleic acids have homology, had well-established utilities at the time of filing. As stated in the Utility Examination Guidelines, "When a class of proteins is defined such that the members share a specific, substantial, and credible utility, the reasonable assignment of a new protein to the class of sufficiently conserved proteins would impute the same specific, substantial, and credible utility to the assigned protein. Likewise, Example 10 of the Revised Interim Utility Guidelines Training Materials indicated that a complete cDNA encoding a protein with homology to DNA ligase, a protein with well-established utility, possessed sufficient utility to meet the statutory requirement. Thus, Applicants identification of the claimed nucleic acids as encoding new members of the classes of Kunitz protease inhibitors, colipases and phosphatidylethanolamine binding proteins is sufficient to satisfy the requirements of 35 U.S.C. §101.

In view of all of the above, Applicants respectfully submit that each of the sequences referred to in the presently-pending claims indeed has patentable utility, both based on the teachings of the specification as filed as well as in view of the knowledge of one of skill in the art at the time of filing. Accordingly, Applicants respectfully request the withdrawal of the rejection of the claims under 35 U.S.C. § 101.

III. Rejections under 35 U.S.C. § 112, first paragraph

Claim 21 was rejected under 35 U.S.C. § 112, first paragraph, for allegedly lacking utility. However, as developed in point II of this answer, Applicants maintain that each of the claims fulfill the utility requirement. Accordingly, Applicants respectfully request the withdrawal of the standing rejection of the claims under 35 U.S.C. § 112, first paragraph.

IV. Rejections under 35 U.S.C. § 112, second paragraph

The Examiner asserts that claim 21 is indefinite because they refer to nucleic acids comprising any of several sequences shown as SEQ ID NOs, or sequences complementary to these sequences. Specifically, according to the Examiner, because the claimed nucleic acid sequences encode proteins, and the two strands of a double stranded nucleic acid encode different protein sequences, then the claim would require both the coding and complementary strands to encode the same protein. As an illustrative example, the Examiner notes that the codon ATG codes for methionine, yet its complement, CAT, codes for histidine. Applicants respectfully traverse this rejection.

The standard for definiteness under 35 U.S.C. §112, second paragraph, is whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity. This determination must be analyzed in view of the content of the application, the teachings of the prior art, and the claim interpretation that one of skill in the art would give. See, e.g. MPEP 2173.02. In the present case, there is no question as to the scope of the claim in question.

The rejected claim 21 is as follows:

A composition comprising: a purified or isolated polynucleotide comprising a nucleotide sequence selected from any one of:

(a) at least 150 consecutive nucleotides of SEQ ID NO:66 or a sequence fully complementary thereto;
(b) at least 150 consecutive nucleotides of SEQ ID NO:76 or a sequence fully complementary thereto;
(c) at least 25 consecutive nucleotides of SEQ ID NO:78 or a sequence fully complementary thereto; or
(d) at least 200 consecutive nucleotides of SEQ ID NO:124 or a sequence fully complementary thereto.

Importantly, the claim makes no reference to whether or not the nucleic acids code for proteins. Regardless of whether or not any of these sequences code for proteins, the scope of every element of this claim is entirely clear. Specifically, one of skill in the art would certainly understand what is meant by, e.g., 150 consecutive nucleotides of SEQ ID NO:166 or a sequence fully complementary thereto. There is no ambiguity regarding this phrase, and the claims are thus definite under § 112, second paragraph.

Further, regarding the fact that the present sequences code for proteins, Applicants submit, first of all, that whether or not these sequences code for proteins has no relevance as to whether a claim is definite under § 112, second paragraph. As discussed supra, there is no question that the subject matter of the claim is clear. Further, Applicants remind the Examiner that the determination of definiteness is made based on the interpretation given by one of skill in the art. Applicants submit that the concept of coding strands and non-coding strands is quite elementary to one of skill in the art, and the present claims would have thus raised no issues of definiteness. Accordingly, the present claims are entirely clear and definite and the present rejection under 35 U.S.C. §112 should be withdrawn.

V. Conclusion

In view of the foregoing, it is submitted that the pending claims are in condition for allowance. Reconsideration and withdrawal of the rejections is respectfully requested. If the Examiner has any questions regarding this matter, she is invited to telephone the undersigned so that the question is resolved.

This response and amendment is being submitted with a request and fee for a 2 month extension of time. Exhibits A-J filed with the Amendment entered Dec. 28, 2000 have been resubmitted along with new Exhibits I-V. Applicant respectfully requests that a timely Notice of Allowance be issued in this case.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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Dated: Aug 24, 2001

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